

Amendments to the Specification:

The additions have been indicated by underling (underlining). The deletions have been indicated by strikethrough (~~strikethrough~~).

Please replace the paragraph which spans page 337 second paragraph to page 338 first paragraph with the following amended paragraph:

Example 35: Specificity of inhibition of certain enzymes by compounds according to the present invention

In order to characterize the specificity of various compounds the following assays were performed. PPIase activity of hPin1, hCyp18, LpCyp18, hFKBP12 and EcParvulin was measured using the protease-coupled PPIase assay according to Fischer et al. (Fischer, G.; Bang, H.; Mech, C. Determination of enzymatic catalysis for the cis-trans-isomerization of peptide binding in proline-containing peptides. [German] Biomed. Biochem. Acta 1984, 43, 1101-1111; Hennig et al., Selective Inactivation of Parvulin-like peptidyl-prolyl cis/trans isomerases by Juglon, Biochemistry. 1998, 37(17):5953-5960). For hPin1 measurements Ac-Ala-Ala-Ser(PO₃H₂)-Pro-Arg-pNA [SEQ ID NO:1] was used as a substrate and trypsin (final concentration 190 µg/ml) as an isomer-specific protease. Activity measurements of other PPIases were made with the substrate peptide Suc-Ala-Phe-Pro-Phe-pNA [SEQ ID NO:2] and the protease -chymotrypsin (final concentration 470 µg/ml). The assays were performed in a final reaction volume of 150 µl at final concentrations of 6 nM hPin1, 10 nM hCyp18, 5 nM LpCyp18, 20 nM EcParvulin and 20 nM hFKBP12, respectively, and 120 µM substrate peptide in 35 mM HEPES (pH 7.8). For inhibition experiments 100-0.01 µM of effector freshly diluted from a DMSO stock solution were added. The amount of solvent was kept constant within each experiment, usually below 0.3% (v/v). All reactions were started by addition of protease. The test was performed by observing the released 4-nitroaniline at 390 nm with a MR5000 UV/Vis spectrophotometer (Dynex) at 6°C. Data were evaluated by calculation of pseudo-first-order rate constants k_{obs} in presence of PPIase and PPIase/effector, respectively, and corrected for the contribution of the non-catalyzed reaction (k_0). Inhibition constants IC₅₀ were calculated using SigmaPlot 8.0 (SPSS).

Please replace the paragraph which spans page 348 second paragraph to page 349 first paragraph with the following amended paragraph:

Example 36: Specificity of inhibition of proteases

In order to investigate the impact of some of the inventive compounds on the activity of key proteases the following assay was performed: Protease activities were measured spectrophotometrically at 30°C according to Schomburg and Salzmann (Schomburg, B.; Salzmann M. GBF: Enzyme Handbook. Springer Verlag, Berlin Heidelberg, 1991) and Bergmeyer et al. (Bergmeyer, H. U.; Bergmeyer, J.; Graßl, M. Methods of Enzymatic Analysis, Vol. V Enzymes 3: Peptides, Proteinases and Their Inhibitors. pp 55 – 371, VCH, Weinheim, 1988). The release of 4-nitroaniline was determined at 390 nm with a Spectramax Plus UV/Vis spectrophotometer (Molecular Devices). The cathepsin B assay was performed in a reaction mixture containing 0.2 µg/ml cathepsin B, 2 mM Z-Arg-Arg-pNA [SEQ ID NO:3] in 88 mM KH₂PO₄, 12 mM Na₂HPO₄, 1.33 mM EDTA, 0.03% Brij 35 (pH 5.8). The trypsin assay was carried out in a reaction mixture containing 0.1 µg/ml trypsin and 120 µM Ac-Ala-Ala-Ser(PO₃H₂) -Pro-Arg-pNA [SEQ ID NO:1] in 35 mM HEPES (pH 7.8) and the papain assay in a mixture consisting of 16 µg/ml papain and 2 mM Bz-DL-Arg-pNA in 10 mM Na₂HPO₄, 2 mM L-Cys, 5 mM EDTA (pH 6.5). In general, reactions were started by addition of peptide substrate after a 30 min incubation of 1-100 µM effector with given concentrations of enzyme.